REMARKS/ARGUMENTS

Claims 13-16, 20-24, 27-32, 36-44, and 48-52 are pending in the present application. The claims remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Bergquist *et al.* (WO 95/14770).

According to the Office Action, this reference discloses a *Thermus filiformis* DNA polymerase allegedly having reverse transcriptase activity in the presence of magnesium and comprising the motif disclosed in SEQ ID NO: 1.

As noted previously, the pending claims are directed to mutated DNA polymerases, which in their native form comprise a polymerase domain comprising the recited sequences. Thus, Bergquist cannot anticipate the present claims unless the recited motif is present in ***the polymerase domain*** of the polymerase disclosed there.

By maintaining this rejection, the Examiner has not taken this element of the claims properly into account. In the second full paragraph of page 4 of the Office Action, the Examiner states that in the absence of an express limitation that the motif occurs at a particular residue, applicants cannot rely on this element of the claim. This is an unnecessarily narrow understanding of the applicants arguments and claims. Applicants' invention does not rely on the precise location of the motif in the claimed polymerase, only that the motif occurs within the polymerase domain of the DNA polymerase enzyme.

As explained previously, one of skill can easily determine the relevant portion of the enzyme by comparison to a DNA polymerase known to comprise the motif in its polymerase domain. Indeed, the specification shows that the location of the motif can be easily determined by comparison of the sequence to a DNA polymerase known to have the motif. The location of the relevant portion of the *T. filiformis* enzyme is identified in Table 1 of the present specification. Table 1 makes clear that the correct motif in the *T. filiformis* enzyme is LSQELSIPYEE, which aligns with similar motifs present in other DNA polymerases. This table was cited in the last response to show that alignment of sequences can be used to identify the proper region of the *T. filiformis* enzyme. The table was ***not*** cited to establish the precise location of the motif in the enzyme.

The relevant motif and region can be seen in the Bergquist *et al.* publication in Figure2, which also provides an alignment with the *T. aquaticus* sequence. The sequence alignment in Bergquist *et al.* reinforces the information provided in Table 1. There it can be seen that LSQELSIPYEE in the *T. filiformis* sequence aligns with LSQELAIPYEE of the *T. aquaticus* sequence. It is clear from both of these comparisons, that the claimed motif present in the *T. filiformis* wild-type enzyme (as is also true for the *T. aquaticus* enzyme) comprises an E at position 4 of the relevant sequence.

Since the Bergquist *et al.* patent application fails to disclose a DNA polymerase with the claimed motif in the polymerase domain, it fails to meet all the limitations of the pending claims. Applicants respectfully request that the rejection be withdrawn.

In the Office Action, the Examiner also dismisses the evidence Applicants have provided to show that Bergquist *et al.* did not actually demonstrate reverse transcription using their enzyme. Rather than reiterating all the evidence provided in the previous response, Applicants wish to respond to a few points made by the Examiner. The Examiner continues to argue that two forward primers are disclosed in Bergquist *et al.* (T7 and P3). The Examiner appears to acknowledge that the T7 primer could not be used to reverse transcribe an mRNA molecule because it is derived from a promoter sequence. The Examiner, however, does not address the evidence provided in the last response that the P3 primer is derived from the human topoisomerase IIb gene despite the assertion by Bergquist *et al.* that mRNA from the human topoisomerase IIa gene was the template in the experiments. Thus, the Examiner has not addressed the fact that ***neither*** of the forward primers disclosed by Bergquist *et al.* could be successfully used in the experiments allegedly described there.

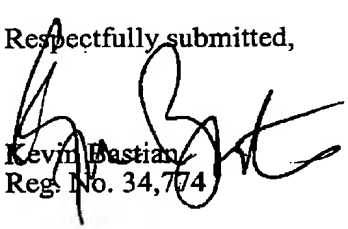
Finally, the Examiner states that even if the Bergquist *et al.* patent application does not show reverse transcription, it does assert that use of magnesium ions are preferable to manganese ions in RT-PCR methods. Applicants respectfully submit a simple statement of the desirability of performing reverse transcription in a magnesium buffer is not sufficient to anticipate the present invention. The present invention is not the recognition that magnesium buffers are preferable, but the development of DNA polymerases that are capable of reverse

transcription in such buffers. In the absence of convincing evidence of such an enzyme, the present rejection is improper and should be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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